

CLAIMS:

1. A cell targeting conjugate comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

5           i)    a DNA minor groove binding ligand incorporating an effective Auger electron-emitting and/or gamma-emitting and/or positron-emitting atom or photoactive moiety;

              ii)    a target cell specific protein or peptide that is capable of internalisation by target cells.

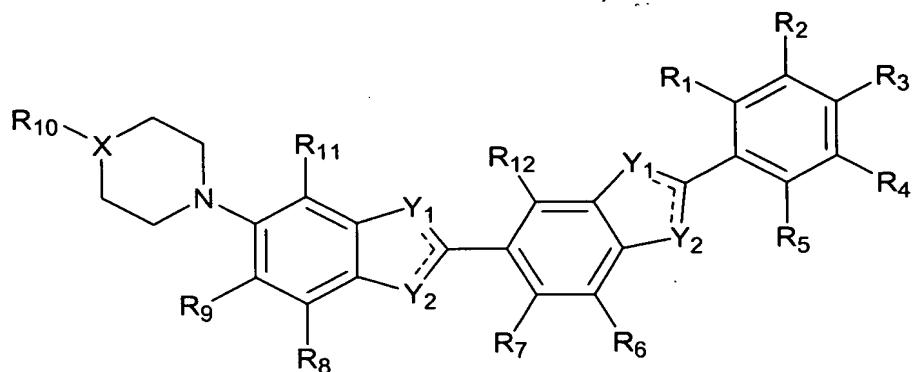
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2. The cell targeting conjugate according to claim 1 wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

15           3. The cell targeting conjugate according to either claim 1 or claim 2 wherein the DNA minor groove binding ligand is selected from lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC1065, naturally occurring antibiotics; and analogues thereof.

20           4. The cell targeting conjugate according to any one of claims 1 to 3 wherein the target cell specific protein or peptide is selected from anti-A33, C595, 4D5, trastuzumab (Herceptin), egf/R3, humanized h-R3, C225 (Erbitux), BrE-3, murine A7, C50, humanized MN-14, anti-A33, MSN-1, bivatuzumab, U36, KIS1, HuM195, anti-CD45, anti-CD19, TXU(anti-CD7)-pokeweed antiviral protein, M195, anti-CD23, apolizumab (Hu1D10), 25          Campath-1H, N901, Ep2, somatostatin analogues, tositumomab (Bexxar), ibritumomab tiuxetan (Zevalin), HB22.7, anti-CD40, OC125, PAM4 and J591.

30           5. The cell targeting conjugate according to any one of claims 1 to 4 wherein the cell targeting conjugate is represented by Formula (I), wherein:



Formula (I)

X is carbon or nitrogen;

Y<sub>1</sub> and Y<sub>2</sub> are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is

5       hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and  
      wherein Y<sub>1</sub> and Y<sub>2</sub> are not both either C(R') or nitrogen;

      --- is a double bond unless the attached Y<sub>1</sub> or Y<sub>2</sub> is N(R'), oxygen or sulfur in which  
      case it is a single bond;

10      R<sub>1</sub> to R<sub>12</sub> are selected from hydrogen, halogen, hydroxy, amino, optionally  
      substituted alkyl, optionally substituted alkenyl, a moiety including a target cell  
      specific protein or peptide, an Auger electron-emitting moiety, a gamma-  
      emitting moiety, a positron-emitting moiety, a photoactive moiety and a  
      cellular uptake inhibiting group, and wherein two of R<sub>1</sub> to R<sub>5</sub> may together  
15      form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least  
      one of R<sub>1</sub> to R<sub>12</sub> comprises a target cell specific protein or peptide, and wherein  
      at least one other of R<sub>1</sub> to R<sub>12</sub> comprises an Auger electron-emitting moiety, a  
      gamma-emitting moiety, a positron-emitting moiety and/or a photoactive  
      moiety;

20      and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or  
      tautomers thereof.

6.      A method of selectively eliminating target cells comprising administering to an  
      environment in which the target cells are located an effective amount of a cell targeting

conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

- 5        i)      a DNA minor groove binding ligand incorporating a cytotoxically effective Auger electron emitting atom;
- ii)     a target cell specific protein or peptide that is capable of internalisation by the target cells.

7.        A method of selectively eliminating target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting

10      conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

- 15        i)      a DNA minor groove binding ligand incorporating a photoactive moiety which when photoactivated generates a species that induces cytotoxic DNA damage;
- ii)     a target cell specific protein or peptide that is capable of internalisation by the target cells;

and exposing the target cells to a source of UV light suitable to initiate formation of the species that induces cytotoxic DNA damage.

20      8.        A method of selectively imaging target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

- 25        i)      a DNA minor groove binding ligand incorporating a gamma-emitting and/or positron-emitting atom;
- ii)     a target cell specific protein or peptide that is capable of internalisation by the target cells;

and detecting and imaging gamma and/or positron emissions from the target cells.

30      9.        The method according to any one of claims 6 to 8 wherein the cell targeting conjugate is administered to an ex-vivo population of cells.

10. The method according to any one of claims 6 to 8 wherein the cell targeting conjugate is administered to a mammalian patient.

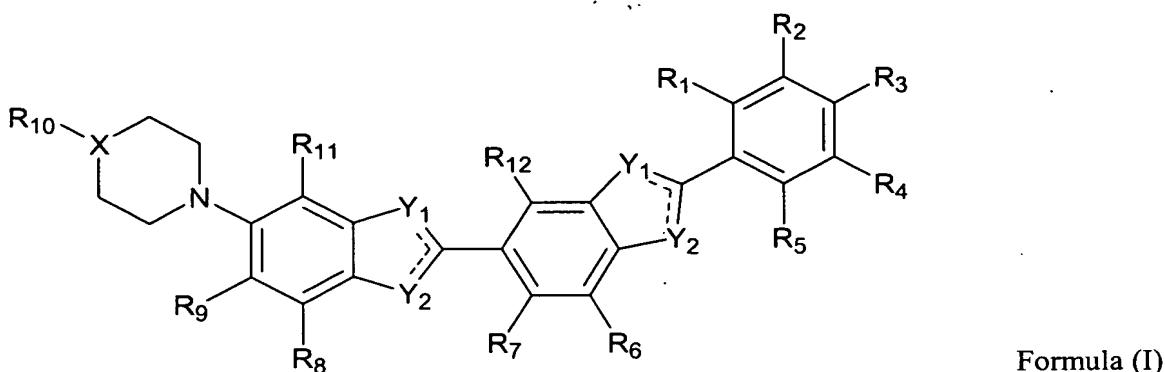
5 11. The method according to any one of claims 6 to 10 wherein the target cells are tumour cells.

12. The method according to any one of claims 6 to 11 wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

10 13. The method according to any one of claims 6 to 12 wherein the target cell specific protein or peptide is selected from anti-A33, C595, 4D5, trastuzumab (Herceptin), egf/R3, humanized h-R3, C225 (Erbitux), BrE-3, murine A7, C50, humanized MN-14, anti-A33, MSN-1, bivatuzumab, U36, KIS1, HuM195, anti-CD45, anti-CD19, TXU(anti-CD7)-15 pokeweed antiviral protein, M195, anti-CD23, apolizumab (Hu1D10), Campath-1H, N901, Ep2, somatostatin analogues, tositumomab (Bexxar), ibritumomab tiuxetan (Zevalin), HB22.7, anti-CD40, OC125, PAM4 and J591.

20 14. The method according to any one of claims 6 to 13 wherein the DNA minor groove binding ligand is selected from lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC1065, naturally occurring antibiotics; and analogues thereof.

25 15. The method according to any one of claims 6 to 13 wherein the cell targeting conjugate is represented by Formula (I), wherein:



X is carbon or nitrogen;

$Y_1$  and  $Y_2$  are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is

5 hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and  
wherein  $Y_1$  and  $Y_2$  are not both either  $C(R')$  or nitrogen;

— is a double bond unless the attached  $Y_1$  or  $Y_2$  is  $N(R')$ , oxygen or sulfur in which case it is a single bond;

$R_1$  to  $R_{12}$  are selected from hydrogen, halogen, hydroxy, amino, optionally

10 substituted alkyl, optionally substituted alkenyl, a moiety including a target cell specific protein or peptide, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R<sub>1</sub> to R<sub>5</sub> may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R<sub>1</sub> to R<sub>12</sub> comprises a target cell specific protein or peptide, and wherein at least one other of R<sub>1</sub> to R<sub>12</sub> comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety and/or a photoactive moiety;

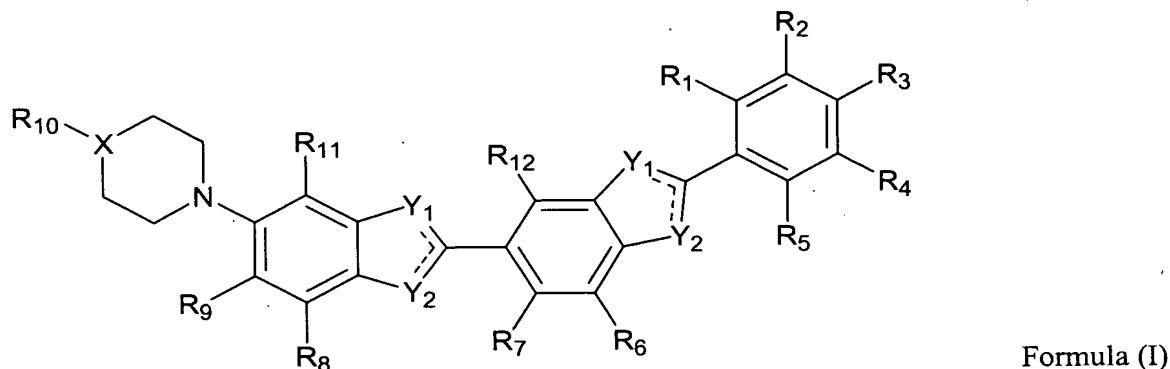
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and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or  
tautomers thereof.

16. The method according to claim 8 wherein the gamma-emitting and/or positron-emitting atom is distanced from a DNA minor groove binding region of the conjugate.

17. A compound according to Formula (I) wherein:

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X is carbon or nitrogen;

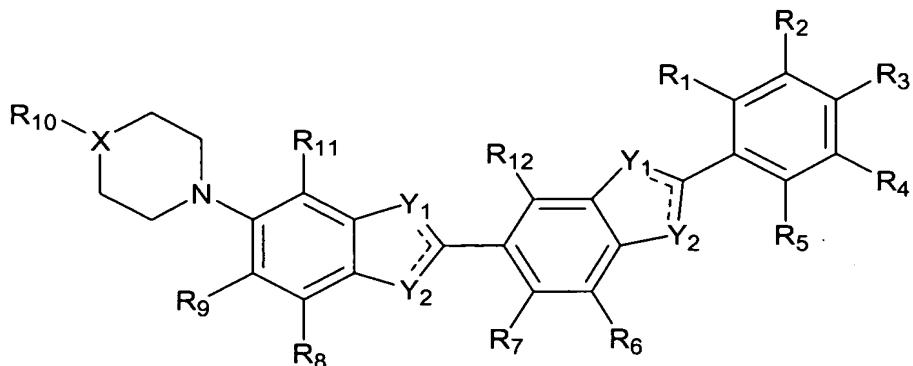
Y<sub>1</sub> and Y<sub>2</sub> are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y<sub>1</sub> and Y<sub>2</sub> are not both either C(R') or nitrogen;

is a double bond unless the attached Y<sub>1</sub> or Y<sub>2</sub> is N(R'), oxygen or sulfur in which case it is a single bond;

R<sub>1</sub> to R<sub>12</sub> are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a leaving group, an activating group, a chelating group and a cellular uptake inhibiting group, and wherein two of R<sub>1</sub> to R<sub>5</sub> may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R<sub>1</sub> to R<sub>12</sub> comprises a carbonyl, carboxylic acid or amino group, and wherein at least one other of R<sub>1</sub> to R<sub>12</sub> comprises a leaving group, an activating group or a chelating group;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

18. A compound according to Formula (I) wherein:



### Formula (I)

5

X is carbon or nitrogen;

$Y_1$  and  $Y_2$  are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is

10 hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and  
wherein  $Y_1$  and  $Y_2$  are not both either  $C(R')$  or nitrogen;

— is a double bond unless the attached  $Y_1$  or  $Y_2$  is  $N(R')$ , oxygen or sulfur in which case it is a single bond;

15  $R_1$  to  $R_{12}$  are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of  $R_1$  to  $R_5$  may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of  $R_1$  to  $R_{12}$  comprises a carbonyl, carboxylic acid or amino group, and wherein at least one other of  $R_1$  to  $R_{12}$  comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety or a photoactive moiety;

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and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.